REMARKS

I. Status of Claims

Claims 1-79 were filed with the application. Claims 9, 10, 24, 28-32 and 57-79 are withdrawn pursuant to a restriction requirement. Thus, claims 1-8, 11-23, 25-27 and 33-56 are under examination and stand rejected, variously, under 35 U.S.C. §112, second paragraph, 35 U.S.C. §103 and over the judicially-created doctrine of obviousness-type double-patenting. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

II. Rejection under 35 U.S.C. §112, Second Paragraph

Claims 1-8, 11-23, 25-27 and 33-56 stand rejected under the second paragraph of §112 as allegedly indefinite. Applicants traverse, but the claims have been amended to clarify the issue of effective amounts. As to whether the method is *in vivo* or *in vitro*, applicants submit that the claims are merely generic to that feature, and they are not indefinite therefor. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

III. Rejection under 35 U.S.C. §103

Claims 1-8, 11-23, 25-27 and 33-56 stand rejected as obvious over Konoplevea I or II in view of Castaigne, Drach or Estey. The examiner argues that both CDDO and retinoids have been shown to treat leukemias, and hence, their combination to treat this same disease would be obvious. Further, the examiner argues that selection of the particular retinoid LGD1069 is obvious as well. Applicants traverse.

First, the examiner has not advanced a proper rejection under §103. There is no discussion of whether one of skill in the art would see any motivation in the cited references for

combination of one drug with the other. The mere fact that they have both been used to treat the same disease is ***not***, in and of itself, sufficient motivation. More importantly, there is no discussion of whether there would be any likelihood of success in such a treatment. Rather, the examiner merely leaps to the alleged lack of surprising results, which is ***only*** relevant where a *prima facie* case has been established.

Second, while the combinations that ***do*** turn out to work may seem logical in hindsight, a proper obviousness analysis requires consideration of the combinations which fail (for toxicity, lack of beneficial effect, *etc.*), of which there are many. It is only through a hindsight analysis, which the examiner applies here, that one can find the prior art to have suggested both the combination, and predicted its likely success. *In re Carroll*, 202 USPQ 571 (CCPA 1979) ("One of the more difficult aspects of resolving questions of non-obviousness is the necessity 'to guard against slipping into the use of hindsight.'"), citing *Graham v. John Deere Co.*, 148 USPQ 459 (U.S. Sup. Ct. 1965). As such, the rejection is improper as a matter of law.

In re Jones, 21 USPQ2d 1941 (Fed. Cir. 1992) dealt with the obviousness of a novel salt of the acid known as dicamba. The PTO alleged that prior art, which disclosed a genus encompassing the salt, rendered a claim to that compound obvious. There, the court found the record lacking with regard to motivation when selecting from such a large number of possibilities:

> Conspicuously missing from this record is any ***evidence***, other than the PTO's speculation (if it can be called evidence) that one of skill in the herbicidal art would have been motivated to make the modifications [to] the prior art salts necessary to arrive at the claimed ... salt."

Jones at 1944 (emphasis in original). The court went on to cite *In re Lalu*, 223 USPQ 1257 (Fed. Cir.) for the same proposition. "The prior art must provide one of ordinary skill in the art the

motivation to make the proposed molecular modifications needed to arrive at the claimed compound." *Lalu* at 1258.

Thus, the prior art, not the examiner or applicant, must provide motivation for selecting a particular species. Here, there are thousands if not millions of possible drug combinations that one might choose for treating leukemias. However, the record is devoid of any evidence, beyond a mere allegation, that would lead one to use CDDO and a retinoid together. As such, appellants submit that this rejection also suffers from the same defect as described in *Jones* — lack of motivation.

In sum, the examiner has not demonstrated that each element of a *prima facie* case – enabling technology, motivation, and likelihood of success – exists here. As such, the rejection is improper and should be withdrawn.

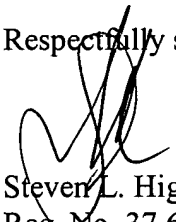
IV. Rejection for Obviousness-Type Double-Patenting

Claim 1 is rejected, provisionally, over claim 37 of U.S. Serial No. 10/435,925. As this rejection is provisional, applicants submit that a proper treatment would be to allow the present case to pass to issue, and advance the rejection in the '925 application.

V. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early indication to that effect is earnestly solicited. The examiner is invited to contact the undersigned attorney at (512) 536-3184 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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